IN THE SECOND CIRCUIT COURT FOR DAVIDSON COUNTY, TENNESSEE
TWENTIETH JUDICIAL DISTRICT AT NASHVILLE

STATE OF TENNESSEE, *ex rel.* ROBERT E. COOPER, JR., ATTORNEY GENERAL and REPORTER,	)	
Plaintiff,	)	**No. 07C227**
v.	)	
BAYER CORPORATION, a foreign corporation,	)	
Defendant.	)	

ORDER MODIFYING AGREED FINAL JUDGMENT

This cause coming before the Court on a Joint Motion to Modify the Agreed Final Judgment, due notice having been given, and the Court being fully advised in the premises,

IT IS HEREBY ORDERED:

1. The Joint Motion To Modify the Agreed Final Judgment is hereby granted;

2. The Agreed Final Judgment entered on January 23, 2007, remains in full force and effect. In addition to the terms contained therein, the Agreed Final Judgment is modified to add the following terms as set forth below which shall be incorporated into the Agreed Final Judgment by this reference as though set forth fully therein:

   a. Section I. Definitions is modified to add Paragraphs X and Y as follows:

i. Paragraph X. "Modification Signatory Attorneys General" shall mean the Attorney General, or his or her designee, of each of the following states that have agreed to this modification of the Agreed Final Judgment: Arizona, Arkansas, California, Connecticut, Delaware, Florida, Idaho, Illinois, Iowa, Kansas, Kentucky, Maine, Maryland, Massachusetts, Michigan, Mississippi, Montana, Nevada, North Carolina, Ohio, Oregon, Pennsylvania, South Dakota, Tennessee, Texas, Washington and Wisconsin.

ii. Paragraph Y. "YAZ®" shall mean the oral contraceptive product composed of a combination of drospirenone and ethinyl estradiol approved for marketing by FDA pursuant to NDAs 21-676, 21-873, and 22-045 under the brand name "YAZ®."

b. Section II. Background is modified to add Paragraphs 6 and 7 as follows:

i. Paragraph 6. Bayer enters into this Modification solely for the purpose of resolving the Modification Signatory Attorneys General's investigation under both the Agreed Final Judgment and their respective states consumer protection statutes into the issues identified in the Warning Letter issued by FDA's Division of Drug Marketing, Advertising, and Communications ("DDMAC") dated October 3, 2008 (attached as Exhibit 1 and hereafter referred to as "Warning Letter"), to avoid unnecessary expense, inconvenience, and uncertainty without admitting any violation of the Agreed

Final Judgment or state consumer protection statutes and without admitting any wrongdoing and for settlement purposes only.

ii. Paragraph 7. This Modification is made without adjudication of any issue of fact or law or finding of wrongdoing or liability of any kind. It is the intent of both Bayer and the Modification Attorneys General that this Modification shall not be admissible in any other matter or proceeding, and shall not bind Bayer in any respect other than in connection with the enforcement of this Modification. Except in an action by the Modification Attorneys General to enforce this Modification, this Modification shall not be construed or used as a waiver or limitation of any defense otherwise available to Bayer or of Bayer's right to defend itself, or make arguments, in any other matter related to the issues identified in the Warning Letter.

c. In addition to the terms contained in the Agreed Final Judgment, "Section XIV. YAZ® Advertising" is added with the following Paragraphs: Pursuant to Tenn. Code Ann. § 47-18-108(a)(4), Bayer is hereby ordered, adjudged and decreed without a cost bond as follows:

i. Bayer shall disseminate corrective advertising that addresses the issues identified in the Warning Letter. The corrective advertising campaign shall consist of a television advertisement and a print advertisement that have been approved by DDMAC and reviewed by the Modification Signatory Attorneys General prior to

submission of this Joint Motion. The television advertisement shall be broadcast on national cable and network television and the print advertisement shall be published in magazines with national distribution. The specific content and timing of this advertising campaign shall be as specified and approved by DDMAC and reviewed by the Modification Signatory Attorneys General prior to the submission of this Joint Motion. Bayer shall spend at least $20 million on this corrective advertising campaign. Bayer's dissemination of the advertising described in this paragraph shall not be construed as an admission by Bayer that the advertisements identified in the Warning Letter were false, misleading, or deceptive in any manner. Nor shall Bayer's dissemination of the advertising described in this paragraph be considered evidence of any liability, wrongdoing, or fault by Bayer.

ii. Bayer agrees to submit all new Direct to Consumer ("DTC") television advertising campaigns for YAZ® to FDA for pre review, wait until Bayer receives a response from FDA prior to running the advertising campaign, and to modify such advertising consistent with any final written comments received from FDA. Non-material modifications to existing advertising campaigns are not covered by this paragraph.

iii. Bayer shall not run print advertising for YAZ suggesting or marketing YAZ®'s effectiveness at treating selected symptoms of

the FDA-approved indication(s) unless the drug's specific FDA-approved indication(s) is/are stated as clearly and conspicuously in the same promotional spread as the symptoms referenced.

iv. Bayer's obligations with respect to paragraphs ii and iii shall remain in effect for six years following the date this Order Modifying Agreed Final Judgment is entered by the court.

v. Bayer shall submit to each Modification Signatory Attorney General on the anniversary of the Effective Date of this Modification a written affirmation setting forth Bayer's compliance with Section XIV.

d. In addition to the terms contained in the Agreed Final Judgment, Section XV RELEASE RE YAZ® is added and with the following paragraphs.

i. Section XV shall pertain to the product YAZ® only and does not alter or modify the release set forth in Section VII of the Agreed Final Judgment.

ii. Based upon their investigation into Bayer's promotional and marketing practices regarding YAZ® and whether those practices violate the Agreed Final Judgment, the Modification Signatory Attorneys General have concluded that the Agreed Final Judgment as modified per this Order Modifying Agreed Final Judgment is the appropriate resolution of any alleged violations of the Agreed Final Judgment by Bayer regarding its marketing and promotion of

the product YAZ® as described by the Warning Letter attached as Exhibit 1 and incorporated by this reference as though set forth in full.

iii. In Consideration of the terms set forth in Section XIV, by execution of this modification of Agreed Final Judgment, each Modification Signatory Attorney General, as defined in Section I, Paragraph X, releases and forever discharges, to the fullest extent permitted by law, Bayer and all of its past and present officers, directors, shareholders, employees, affiliates, subsidiaries, predecessors, assigns and successors (hereinafter referred to collectively as the "Released Parties"), from contempt proceedings that were or could have been asserted against the Released Parties by the Modification Signatory Attorneys General for the marketing and promotion of YAZ® by engaging in only the specific conduct described in the Warning Letter attached hereto as Exhibit 1 and incorporated by this reference as though set forth in full.

iv. The Modification Signatory Attorneys General also release and forever discharge, to the fullest extent permitted by law, the Released Parties from any other claims or causes of action under the following consumer protection statutes: ARIZONA - Consumer Fraud Act, A.R.S. § 44-1521, et seq.; ARKANSAS - Deceptive Trade Practices Act, Ark. Code Ann. § 4-88-101 et seq.; CALIFORNIA - Bus. & Prof. Code, § 17200 et seq.;

CONNECTICUT - Connecticut Unfair Trade Practices Act, Conn. Gen. Stat. § 42-110a et seq.; DELAWARE - Delaware Consumer Fraud Act, 6 Del. C. § 2511, et seq. and Deceptive Trade Practices Act, 6 Del. C. §2532 et seq.; FLORIDA - Deceptive and Unfair Trade Practices Act, Fla. Stat. Ch. 501.201 et seq.; IDAHO - Consumer Protection Act, Idaho Code § 48-601 et seq.; ILLINOIS - Consumer Fraud and Deceptive Business Practices Act, 815 ILCS § 505/1 et seq.; IOWA - Iowa Consumer Fraud Act, Iowa Code Section 714.16; KANSAS - Consumer Protection Act, K.S.A. 50-623 et seq.; KENTUCKY - Consumer Protection Statute, KRS 367.170; MAINE - Unfair Trade Practices Act, 5 M.R.S.A. § 205-A et seq.; MARYLAND - Consumer Protection Act, Md. Code Ann., Com. Law § 13-101 et seq.; MASSACHUSETTS - Consumer Protection Act, M.G.L. c. 93A et seq.; MICHIGAN - Consumer Protection Act, Mich. Comp. Laws § 445.901 et seq.; MISSISSIPPI - Consumer Protection Act, Miss. Code Ann. § 75-24-1 et seq.; MONTANA -Mont. Code Ann. § 30-14-101 et seq.; NEVADA - Deceptive Trade Practices Act, Nevada Revised Statutes 598.0903 et seq.; NORTH CAROLINA - Unfair and Deceptive Trade Practices Act, N.C. Gen. Stat. § 75-1.1 et seq.; OHIO - Consumer Sales Practices Act, R.C. 1345.01 et seq.; OREGON - Unlawful Trade Practices Act, ORS 646.605 to 646.656; PENNSYLVANIA - Unfair Trade Practices and

Consumer Protection Law, 73 P.S. § 201-1 et seq.; SOUTH DAKOTA - Deceptive Trade Practices Act, S.D. Codified Laws § 37-24, et seq.; TENNESSEE - Tennessee Consumer Protection Act, Tenn. Code Ann. §§ 47-18-101 et seq.; TEXAS - Deceptive Trade Practices - Consumer Protection Act, Tex. Bus. and Com. Code § 17.47, et seq.; WASHINGTON - Unfair Business Practices/Consumer Protection Act, R.C.W. 19.86 et seq.; WISCONSIN - Wis. Stat. § 100.18 et seq. (Fraudulent Representations) and Wis. Stat. § 100.182 et seq. (Fraudulent Drug Advertising) that were or could have been asserted against the Released Parties by the Modification Signatory Attorneys General for the marketing and promotion of YAZ® by engaging in only the specific conduct described in the Warning Letter attached hereto as Exhibit 1 and incorporated by this reference as though set forth in full. This release does not extend to conduct or advertisements by the Released Parties that were not specifically described in the Warning Letters attached hereto as Exhibit 1 including, but not limited to, conduct that occurred prior to or subsequent to the described conduct, conduct pertaining to advertisements not addressed in the Warning Letter, or conduct beyond the scope of what is described in the Warning Letter.

e. Notwithstanding any term of this Modification, specifically reserved and

excluded from the Released Claims as to any entity or person, including Released Parties, are any and all of the following:

i. Any criminal liability that any person or entity, including Released Parties, has or may have to any or all of the Signatory Attorneys General;

ii. Any civil or administrative liability that any person or entity, including Released Parties, has or may have to any or all of the Signatory Attorneys General, under any statute, regulation or rule not expressly covered by the release in Paragraph iii. above, including, but not limited to, any and all of the following claims:

1. State or federal antitrust violations;
2. Reporting practices, including "best price," "average wholesale price" or "wholesale acquisition cost";
3. Medicaid violations, including federal Medicaid drug rebate statute violations, Medicaid fraud or abuse, and/or kickback violations related to any State's Medicaid program;
4. State false claims violations; and,
5. Claims to enforce the terms and conditions of this Modification.

iii. Any liability under the above-cited consumer protection laws of any or all of the Modification Signatory Attorneys General which any person or entity, including Released Parties, has or may have

to individual consumers or State program payors of said Individual States, and which have not been specifically enumerated as included herein.

3. Defendant hereby waives any and all rights which it may have to be heard in connection with judicial proceedings regarding entry of the Order Modifying Agreed Final Judgment.

4. This Order Modifying Agreed Final Judgment and the Agreed Final Judgment shall only be enforceable by the parties to this action.

5. All costs associated with the Joint Motion and this Order Modifying Agreed Final Judgment and any other incidental costs or expenses incurred thereby shall be borne by Defendant. No costs shall be taxed against the State as provided by Tenn. Code Ann. § 47-18-116.

6. The Clerk is ordered to enter this Order Modifying Agreed Final Judgment forthwith.

IT IS SO ORDERED.

HONORABLE AMANDA MCCLENDON

JOINTLY APPROVED AND
SUBMITTED FOR ENTRY:

FOR PLAINTIFF, STATE OF TENNESSEE:

ROBERT E. COOPER, JR.
Attorney General and Reporter
B.P.R. No. 10934

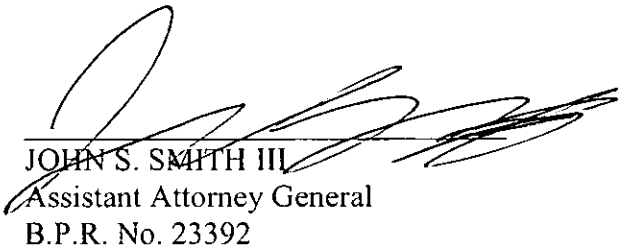

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EXHIBIT 1

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

TRANSMITTED BY FACSIMILE

Reinhard Franzen
President & Chief Executive Officer
Bayer HealthCare Pharmaceuticals, Inc.
P.O. Box 1000
Montville, NJ 07045-1000

Re: NDA # 21-676, 21-873, 22-045
YAZ® (drospirenone and ethinyl estradiol) Tablets
MACMIS ID# 16473

WARNING LETTER

Dear Mr. Franzen:

The Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed two 60-second direct-to-consumer (DTC) broadcast television advertisements (TV Ads) entitled "Not Gonna Take it" (ZYRA-6323) and "Balloons" (ZYRA-6567) for YAZ® (drospirenone and ethinyl estradiol) Tablets (YAZ) submitted by Bayer HealthCare Pharmaceuticals, Inc. (Bayer) under cover of separate Forms FDA-2253. The TV Ads are misleading because they broaden the drug's indication, overstate the efficacy of YAZ, and minimize serious risks associated with the use of the drug. Thus, the TV Ads misbrand the drug in violation of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. 352(n), 352(f)(1) & 321(n), and FDA's implementing regulations. 21 CFR 201.100(c)(1); 201.128; 202.1(e)(5)(iii) & (e)(6)(i). These violations are concerning from a public health perspective because they encourage use of YAZ in circumstances other than those in which the drug has been approved, over-promise the benefits and minimize the risks associated with YAZ.

Background

According to the INDICATIONS AND USAGE section from the FDA-approved product labeling (PI), YAZ is approved for the following indications (in pertinent part):

> [F]or the prevention of pregnancy in women who elect to use an oral contraceptive. . . .
>
> [F]or the treatment of symptoms of premenstrual dysphoric disorder (PMDD) in women who choose to use an oral contraceptive as their method of contraception. The effectiveness of YAZ for PMDD when used for more than three menstrual cycles has not been evaluated.

> The essential features of PMDD according to the Diagnostic and Statistical Manual-4th edition (DSM-IV) include markedly depressed mood, anxiety or tension, affective lability, and persistent anger or irritability. Other features include decreased interest in usual activities, difficulty concentrating, lack of energy, change in appetite or sleep, and feeling out of control. Physical symptoms associated with PMDD include breast tenderness, headache, joint and muscle pain, bloating and weight gain. In this disorder, these symptoms occur regularly during the luteal phase and remit within a few days following onset of menses; the disturbance markedly interferes with work or school, or with usual social activities and relationships with others. Diagnosis is made by healthcare providers according to DSM-IV criteria, with symptomatology assessed prospectively over at least two menstrual cycles. In making the diagnosis, care should be taken to rule out other cyclical mood disorders.
>
> **YAZ has not been evaluated for the treatment of premenstrual syndrome (PMS)** [emphasis added].
>
> [F]or the treatment of moderate acne vulgaris in women at least 14 years of age, who have no known contraindications to oral contraceptive therapy and have achieved menarche. YAZ should be used for the treatment of acne only if the patient desires an oral contraceptive for birth control.

Additionally, the BRIEF SUMMARY PATIENT PACKAGE INSERT and DETAILED PATIENT PACKAGE INSERT state that:

> . . . YAZ has not been shown to be effective for the treatment of premenstrual syndrome (PMS), a less serious cluster of symptoms occurring before menstruation. If you or your healthcare provider believes you have PMS, you should only take YAZ if you want to prevent pregnancy; and not for the treatment of PMS. . . .

The PI for YAZ includes a BOXED WARNING that states (in pertinent part):

Cigarette smoking increases the risk of serious cardiovascular side effects from oral contraceptive use. This risk increases with age and with heavy smoking (15 or more cigarettes per day) and is quite marked in women over 35 years of age. Women who use oral contraceptives should be strongly advised not to smoke.

Additionally, there are numerous warnings associated with the use of YAZ including, but not limited to, venous and arterial thrombotic and thromboembolic events (such as myocardial infarction, thromboembolism, stroke), hepatic neoplasia, gallbladder disease, and hypertension.

Moreover, YAZ has additional risks because it contains the progestin, drospirenone. Drospirenone has antimineralocorticoid properties which can lead to hyperkalemia in high risk patients, which may result in potentially serious heart and health problems. Women taking YAZ must be concerned about the drug interactions that could increase potassium, in addition to the drug interactions common to all combination oral contraceptives. This additional risk is described in the bolded WARNINGS section of YAZ's PI.

Broadening of Indication

Premenstrual Dysphoric Disorder (PMDD)

"Not Gonna Take It" (ZYRA-6323) & "Balloons" (ZYRA-6567)

The TV Ads misleadingly suggest that YAZ is effective in a broader range of patients and conditions than has been demonstrated by substantial evidence or substantial clinical experience. Specifically, given the overlap in certain symptoms between premenstrual syndrome (PMS) and PMDD, and the material limitation on YAZ's PMDD indication (that it has not been evaluated for the treatment of the less serious condition, PMS), the TV Ads misleadingly suggest that YAZ is appropriate for treating women with PMS, who may not be appropriate candidates for this drug. We note that despite listing certain symptoms of PMDD, nowhere do the TV Ads use the full phrase "premenstrual dysphoric disorder," to more completely distinguish PMDD from PMS, thereby increasing the likelihood that a viewer, in light of the claims and presentations described below, will understand it to be the same as, or substantially similar to, PMS.

The TV Ad "Not Gonna Take It" starts by stating:

- "We all know that birth control pills are 99% effective and can give you shorter, lighter periods. But did you know there's a Pill that could do more?"

It then displays images of energetic, euphoric, playful women singing "We're Not Gonna Take It" as they kick, punch, and push words describing symptoms such as "IRRITABILITY," "MOODINESS," "BLOATING," and "FEELING ANXIOUS," away from the screen, followed by the claim "It's YAZ! And there's no other birth control like it." The screen then displays a listing of symptoms including: irritability; increased appetite; moodiness; fatigue; feeling anxious; headaches; bloating; and muscle aches.

Similarly, the TV Ad "Balloons" starts by stating:

- "All birth control pills are 99% effective and can give you shorter, lighter periods. But there's one Pill that goes beyond the rest. It's YAZ."

It then displays numerous balloons throughout the ad with symptoms, such as, "IRRITABILITY," "MOODINESS," "FEELING ANXIOUS," "BLOATING," "FATIGUE;" "MUSCLE ACHES," "HEADACHES," "INCREASED APPETITE," and "ACNE."

The symptoms displayed in these ads are commonly seen in women with PMS, which is a less serious and more common condition than PMDD. PMDD is a disorder whose hallmarks

include markedly depressed mood, anxiety or tension, affective lability, and persistent anger or irritability. Other features of PMDD include decreased interest in usual activities, difficulties concentrating, lack of energy, change in appetite or sleep, and feeling out of control. As discussed in the PI, for a diagnosis of PMDD:

> ...the disturbance markedly interferes with work or school, or with usual social activities and relationships with others. Diagnosis is made by healthcare providers according to the DSM-IV criteria, with symptomatology assessed prospectively over at least two menstrual cycles. In making the diagnosis, care should be taken to rule out other cyclical mood disorders.

The TV Ads entirely omit the material limitation from the PI of the drug's PMDD indication – i.e., that "YAZ has not been evaluated *for the* treatment of premenstrual syndrome (PMS)" – and fail to convey that the drug is only indicated for women who experience the symptoms presented to such a degree that they have PMDD, rather than PMS. As a result of the failure to convey these material facts, and the failure to explain what PMDD is, in contrast to PMS, the TV Ads misleadingly suggest that YAZ is approved to treat women with any severity of the symptoms presented, regardless of whether their symptoms are actually severe enough to constitute PMDD.

We note that the list of symptoms displayed in the TV Ads are accompanied by the text "YAZ treats PMDD" along with a SUPER reading "PMDD is a mood disorder related to the menstrual cycle." However, these disclosures do not suffice to communicate the material fact that YAZ is not approved for treatment of PMS or to overcome the implication created by the totality of the visuals and images in the ads that YAZ is appropriate for any woman who experiences the symptoms presented. We also note that the voiceover states that "YAZ is the only birth control pill proven to treat the emotional and physical premenstrual symptoms that are severe enough to impact your life." However, this claim also fails to communicate that YAZ is not approved for treatment of PMS, and fails to distinguish between PMS and PMDD.

The totality of the visual and audio presentations in both TV ads suggest that YAZ is approved to treat women with any severity of the symptoms presented, including women with PMS, when this is not the case. Thus, the TV Ads misleadingly broaden the indication of the drug.

Acne

In addition, the TV Ads suggest that YAZ is approved for acne of all severities when this is not the case. Specifically, in "Not Gonna Take it," the word "ACNE" appears in large print in the middle of the screen along with the audio claim "*It can* also help keep your skin clear," which is accompanied by a close-up visual of a woman with completely clear skin. Similarly, in "Balloons," the "ACNE" balloon is prominently displayed on the screen, as it floats by a smiling woman with obviously clear skin, along with the audio claim that YAZ "...also helps keep skin clear." These presentations fail to adequately convey that, as noted in the PI, "YAZ is indicated for the treatment of moderate acne vulgaris..." (emphasis added). While the TV Ads do include a SUPER which refers to "improvement in ... moderate acne" in small,

unbolded print, this does not mitigate the misleading impression created by the prominent audio and visual claims in the TV Ads that YAZ is indicated for acne of all severities.

Overstatement of Efficacy

PMDD

"Balloons" (ZYRA-6567)

The TV Ad is misleading because it suggests that YAZ is more effective than has been demonstrated by substantial evidence or substantial clinical experience. The totality of the audio and visual claims and presentations misleadingly suggests that treatment with YAZ will allow women to say "good-bye" to their symptoms completely. For example, the TV Ad's theme song "Good-Bye to you" plays in the background as energetic, euphoric, playful women release balloons into the air displaying certain symptoms (e.g., irritability, moodiness, feeling anxious, bloating, fatigue, muscle aches, headaches, increased appetite, and acne). The balloons then float up and away from the women misleadingly suggesting that these women are saying, "goodbye" to their symptoms and are now symptom-free, when such an elimination of symptoms has not been demonstrated by substantial evidence or substantial clinical experience. According to the PI, in the primary clinical trial that served as the basis for approval of YAZ in the PMDD population, "...the average decrease (improvement) from baseline was 37.5 points in women taking YAZ, compared to 30.0 points in women taking placebo" (added emphasis). These results do not support the implication that YAZ will result in a complete cessation of PMDD symptoms.

Acne

"Not Gonna Take It" (ZYRA-6323) & "Balloons" (ZYRA-6567)

The TV Ads include close-up images of women with completely clear, acne-free skin. In the TV Ad "Not Gonna Take It," there is an image of a woman with the word "ACNE" prominently displayed on the screen before the word "ACNE" fades away from view. The woman turns her face to the side showing viewers that she has no visible signs of acne on her face, in conjunction with the audio claim "It can also help keep your skin clear." In "Balloons," a woman with obviously clear skin smiles and acknowledges the "ACNE" balloon as it floats away from the center of the screen and disappears into the sky, in conjunction with, the background song "Good-bye to you" and the audio claim that YAZ "...also helps keep skin clear." The overwhelming impression conveyed by the TV Ads is that treatment with YAZ results in clear, acne-free skin for those women suffering from acne when this has not been demonstrated by substantial evidence or substantial clinical experience. As illustrated by Table III in the PI, the percentage of subjects assessed by the Investigator's Static Global Assessment (ISGA) with a 'clear' or 'almost clear' rating at day 15 of cycle 6 was 15% and 21% for subjects receiving YAZ versus 4% and 9% of placebo subjects in Studies 1 and 2, respectively. Furthermore, the mean percent reduction of total lesions at day 15 of cycle 6 was 42% and 46% for subjects receiving YAZ versus 25% and 31% of placebo subjects in studies 1 and 2, respectively. Although these results are significant, they do not demonstrate that YAZ results in clear, acne-free skin for a typical woman; rather, these results demonstrate that it reduces the amount of acne lesions more than placebo but does not

result in completely clear skin for these women. Thus, the TV Ads misleadingly overstate the efficacy of the drug.

Minimization of Risk

"Not Gonna Take It" (ZYRA-6323) & "Balloons" (ZYRA-6567)

The audio communication of serious risk disclosures during the "major statement" is minimized by distracting visuals, numerous scene changes, and other competing modalities such as the background music which combine to interfere with the presentation of the risk information. In "Not Gonna Take It", the fast-paced visuals depict various women looking at pictures, trying on clothes, chatting at a cafe, stretching/exercising in a park, and walking down the street while the audio component describes the major risks associated with YAZ. Similarly, in "Balloons," the background music plays as fast-paced visuals depict various women running in a park, sitting on a scenic waterfront, smiling, walking out of a coffee shop, driving and singing, walking out on a balcony, using an elevator, walking through the street to join friends, in addition, to a pigeon on a building ledge and balloons being released and floating away. These complex presentations distract from and make it difficult for viewers to process and comprehend the important risks being conveyed. This is particularly troubling as some of the risks being conveyed are serious, even life-threatening. The overall effect of the distracting visuals, graphics, concurrent supers and background music is to undermine the communication of important risk information, minimizing these risks and misleadingly suggesting that YAZ is safer than has been demonstrated by substantial evidence or substantial clinical experience.

Conclusion and Requested Action

For the reasons discussed above, the promotional piece misbrands YAZ in violation of the Act, 21 U.S.C. 352(n), 352(f)(1), & 321(n), and FDA implementing regulations. 21 CFR 201.100(c)(1); 201.128; 202.1(e)(5)(iii) & 202.1(e)(6)(i).

DDMAC asks Bayer to immediately cease dissemination of violative promotional materials for YAZ that are the same as or similar to those described above. Please submit a written response to this letter on or before October 20, 2008, describing your intent to comply with this request, listing all promotional materials for YAZ that are the same as or similar to those described above, and explaining your plan for discontinuing use of such materials. Because the violations described above are serious, we request, further, that your submission include a comprehensive plan of action to disseminate truthful, non-misleading, and complete corrective messages about the issues discussed in this letter to the audience(s) that received the violative promotional materials. Please direct your response to me at the Food and Drug Administration, Center for Drug Evaluation and Research, Division of Drug Marketing, Advertising, and Communications, 5901-B Ammendale Road, Beltsville, MD 20705-1266, facsimile at (301) 847-8444. In all future correspondence regarding this matter, please refer to MACMIS ID # 16473 in addition to the NDA number(s). If you choose to revise your promotional materials, DDMAC is willing to assist you with your revised materials by commenting on your revisions before you use them in promotion. We remind you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for YAZ comply with each applicable requirement of the Act and FDA implementing regulations. Failure to correct the violations discussed above may result in FDA regulatory action, including seizure or injunction, without further notice.

Sincerely,

{See appended electronic signature page}

Thomas Abrams, R.Ph., M.B.A.
Director
Division of Drug Marketing,
Advertising, and Communications

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Thomas Abrams
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